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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,525	02/27/2004	Richard James Cawthray	02911.012130.	7746

5514 7590 03/31/2011

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EXAMINER	
ROBERTS, LEZAH	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
03/31/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,525	CAWTHRAY ET AL.	
	Examiner	Art Unit	
	LEZAH ROBERTS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,11,14,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,11,14,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed September 8, 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims

Claim Rejections - 35 USC § 103 – Obviousness

1) Claims 1, 2, 4, 11, 14, 25 and 26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Daifotis et al. (US 5,994,329) in view of Kelly (US 4,817,819) in further view of Palo Alto Medical Foundation (January 2002).

Applicant asserts the kit of the instant claims combines administration of an active with a nutrient while it provides a means wherein simultaneous dosing of the bisphosphonate and the nutrient is avoided. This combined administration increases the benefits achieved by the treatment since osteoporosis treatments are less effective in

individuals with calcium and vitamin D deficiency. The subject kit also increases patient compliance and ease of administration. Whereas with conventional kits, patients may forget or simply not follow instructions regarding when to take the active versus when to take the nutrient, with the subject invention, administration is simplified and clarified. Still further, since bisphosphonate and calcium should not be taken at the same time because the calcium interferes with absorption of the active (page 2, lines 28-38), the kit clearly teaches patients to take the accompanying nutrient on days only when not taking the active, thereby avoiding any problems associated with simultaneous dosing. Id.

The Examiner submits that the disclosure of Daifotis provides the means for avoiding simultaneous dosing of the bisphosphonate and the nutrient by disclosing the nutrient is taken on the days the bisphosphonate is not. Although it does not disclose the benefits of such dosing, it does clearly suggest the regimen. Further patient compliance and ease of administration would be achieved based on the teachings of Daifotis because Daifotis suggest packaging that would allow a patient to keep track of when to take the disclosed bisphosphonates.

Applicant argues Daifotis is directed toward a method for inhibiting bone resorption employing a bisphosphonate according to a continuous schedule. As acknowledged by the Examiner, Daifotis fails to teach or suggest a blister pack as disclosed in the present invention.

The Examiner disagrees and submits that although Daifotis does not explicitly disclose the blister pack in the configuration recited by the instant claims, wherein the

bisphosphonate is in a row in the first position followed by a supplement in positions 2-7, it does suggest the configuration by disclosing a kit as blister pack. It is disclosed the blister pack may have a memory aid that can be provided in the form of numbers, letters or other markings or with a calendar insert designating the days in the treatment schedule in which the dosages can be administered. Placebo dosages, or calcium or dietary supplements, either in a form similar to or distinct from the bisphosphonate dosages, can be included to provide a kit in which a dosage is taken every day. This indicates that the calcium supplement is not taken on the same day as the bisphosphonate, which would lead one of ordinary skill in the art to the instant invention.

Applicant further argues, while Daifotis discloses the use of a bisphosphonate according to varying dosing schedules, it fails to specifically recite or suggest, by way of example, any regimens administering doses of a nutrient, and fails to teach or suggest the amount of calcium or other nutrient that might be administered in unit doses in the kit. Daifotis discloses a list of possible additional dosages to the kit, including calcium, as a potential memory aid, however, it fails to specifically identify vitamins, or, more specifically, vitamin D. Daifotis simply fails to teach or suggest the kit of the present invention and fails to appreciate the benefits achieved by the present invention as explained above and in the Declaration. Therefore, for all of the reasons set forth above, Applicants submit that Daifotis fails to render the presently claimed invention obvious.

The Examiner disagrees and submits that Daifotis is clear in its disclosure of regimens for administering the bisphosphonates with a nutrient. The reference discloses

that the nutrients are used on days when the bisphosphonates are not. This is in order to help the patient stay on schedule when using a bisphosphonate regimen. Further the claims do not require vitamin D. The claims recite the nutrient is selected from calcium, calcium and vitamin D, and a combined unit dose of calcium and vitamin D. Therefore the references do not need disclose vitamin D. The reference does disclose calcium as a nutrient taken on the days that the bisphosphonate is not and therefore meets the limitation of the instant claims. The Declaration will be discussed in the Declaration section below.

Applicant further argues Kelly fails to remedy the deficiencies of Daifotis. Kelly does not teach administration of unit doses of an accompanying calcium, vitamin D, or a nutrient of any kind. It merely teaches that tablets in the blister pack might be a placebo or non-active tablet. Further, there is clearly no disclosure or suggestion of the amount of calcium, or vitamin D to be administered in the unit doses as presently claimed, e.g., about 400 mg to about 1500 mg of elemental calcium per day and about 100 IU to 10,000 IU per day.

The Examiner submits that in regard to Kelly, it is used to show that blister packs such as those recited by the instant claims are known in the art. Placebos are often used as place holders to insure that a patient takes the prescribed medication on the appropriate day and time intervals. Therefore one of ordinary skill in the art would be motivated to use a blister pack having placebo, or in the instant case, nutrients to insure a patient taking bisphosphonates stayed on the prescribed schedule. In regard to the

dosage of vitamin D and calcium, this deficiency is cured by Palo Alto Medical Foundation.

Applicant further asserts, Kelly does not teach or suggest the importance of correct dosing of the bisphosphonate and the nutrient, as fully explained in the Declaration, avoidance of simultaneous daily dosing, or the advantages and superior results achieved by using the kit of the present invention. Therefore, Applicants respectfully submit that Daifotis and Kelly, in any permissible combination, fail to render the present invention obvious.

The Examiner submits that Daifotis discloses the importance of correct dosing of the bisphosphonate and the advantages of using a blister pack, by disclosing the use of blister packs, memory aids and placebos, such as nutrients including calcium, to insure patient compliance. Therefore hindsight reasoning was not used because the use of blister packs with memory aids and nutrients to take on days where the bisphosphonate was not taken was clearly suggested by Daifotis. Therefore the combination of references renders the invention of the instant claims obvious.

Applicant argues that Palo Alto Medical Foundation fails to remedy the deficiencies of Daifotis and Kelly. Palo Alto Medical Foundation fails to specify a kit containing an active ingredient, and fails to offer any guidance on the dosing of the active in relation to the supplement and the benefits that may be achieved by a kit whereby simultaneous dosing is avoided. Accordingly, Applicants respectfully submit

that Daifotis, Kelly and Palo Alto Medical Foundation, in any permissible combination, fail to render the present invention obvious and respectfully request withdrawal of the § 103 rejections.

The Examiner submits that Daifotis suggests the use of calcium as a supplement taken on days when the bisphosphonate are not taken. Thus the primary reference discloses not taking the calcium supplement on the same day as the bisphosphonate. Thus hindsight reasoning was not used for the basis of the rejection. The Palo Alto Medical Foundation was used to disclose the recommended dosages when taking calcium and vitamin D. These dosages overlap those recited by the instant claims. One of ordinary skill in the art would be motivated to use these dosages when combining calcium or vitamin D in a blister pack with a bisphosphonate, as suggested by the combination of Daifotis and Kelly because are recommended dosages for particular supplements.

2) Claims 1, 2, 4, 11, 14, 25 and 26 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Daifotis et al. (US 5,994,329) in view of Allendorf et al. (US 5,265,728) in further view of Palo Alto Medical Foundation (January 2002).

See Applicant's arguments above in regard to Daifotis et al. and Palo Alto Medical foundation.

See Examiner's responses above in regard to Daifotis et al. and Palo Alto Medical Foundation.

Applicant asserts Allendorf et al. fail to remedy the deficiencies of Daifotis. Allendorf does not teach administration of unit doses of an accompanying calcium, vitamin D, or a nutrient of any kind. It merely teaches that seven tablets in the blister pack might be a placebo or non-active tablet. Further, there is clearly no disclosure or suggestion of the amount of calcium, or vitamin D to be administered in the unit doses as presently claimed, e.g., about 400 mg to about 1500 mg of elemental calcium per day and about 100 IU to 10,000 IU per day.

The Examiner submits that in regard to Allendorf et al., it is used to show that blister packs such as those recited by the instant claims are known in the art. Placebos are often used as place holders to insure that a patient takes the prescribed medication on the appropriate day and time intervals. Therefore one of ordinary skill in the art would be motivated to use a blister pack having placebo, or in the instant case, nutrients to insure a patient taking bisphosphonates stayed on the prescribed schedule. In regard to the dosage of vitamin D and calcium, this deficiency is cured by Palo Alto Medical Foundation.

Applicant further asserts, Allendorf et al. do not teach or suggest the importance of correct dosing of the bisphosphonate and the nutrient, as fully explained in the Declaration, avoidance of simultaneous daily dosing, or the advantages and superior

results achieved by using the kit of the present invention. Therefore, Applicants respectfully submit that Daifotis and Allendorf et al., in any permissible combination, fail to render the present invention obvious.

The Examiner submits that Daifotis discloses the importance of correct dosing of the bisphosphonate and the advantages of using a blister pack, by disclosing the use of blister packs, memory aids and placebos to insure patient compliance. Therefore the use of blister packs with memory aids and nutrients to take on days where the bisphosphonate was not taken was clearly suggested by Diafotis. The combination of references renders the invention of the instant claims obvious.

Applicant argues that Palo Alto Medical Foundation fails to remedy the deficiencies of Daifotis and Al. Palo Alto Medical Foundation fails to specify a kit containing an active ingredient, and fails to offer any guidance on the dosing of the active in relation to the supplement and the benefits that may be achieved by a kit whereby simultaneous dosing is avoided. Accordingly, Applicants respectfully submit that Daifotis, Kelly, Allendorf and Palo Alto Medical Foundation, in any permissible combination, fail to render the present invention obvious and respectfully request withdrawal of the § 103 rejections.

The Examiner submits that Daifotis suggests the use of calcium as a supplement taken on days when the bisphosphonate is not taken. Thus the primary reference discloses not taking the calcium supplement on the same day as the bisphosphonate. Thus hindsight reasoning was not used for the basis of the rejection. Thus the instant

claims are obvious over the combined teachings of Daifotis, Allendorf and Palo Alto Medical Foundation.

Declaration by Stefan Van Der Geest

The declaration filed on February 7, 2011 by Stefan Van Der Geest explains that there is a problem in the field of osteoporosis treatment and postmenopausal osteoporotic women take their calcium-containing nutrient and/or other medication incorrectly in relation to the bisphosphonate. When a bisphosphonate is taken concurrently with a calcium product, the bisphosphonate is completely ineffective. It is also disclosed that some patients took the bisphosphonate with food and liquids other than water, which is not recommended. This demonstrates that patients often do not comply with the dosing instructions. It is further emphasized that there is a need to address the problems of patient compliance with dosing instructions. The claimed invention is specifically invented and designed to facilitate correct dosing to increase the likelihood that postmenopausal osteoporotic patients will receive both a calcium-containing nutrient and risedronate, thereby providing better treatment to patients in need. The present invention does not contain a calcium-containing tablet on the day of the bisphosphonate intake but, for the rest of the week, it contains 6 (or 12) calcium-containing tablets.

The Examiner submits that although the problem of patient compliance is not disclosed by Daifotis, Daifotis does disclose not taking calcium on the same day as the

bisphosphonate and therefore the bisphosphonates of Daifotis would not be rendered ineffective. It would also appear that Daifotis addresses the need for patient compliance with dosing instructions by suggesting using blister packs and memory aids. Daifotis also discloses using the supplements on the days when bisphosphonate is not taken. The secondary references of Kelly and Allendorf actually disclose a blister pack comprising the prescribed medicine and placebo. Therefore one of ordinary skill in the would be motivated to use a placebo, in the case of Daifotis, calcium, in a blister pack along with the prescribed bisphosphonate medicine in order to aid a patient with complying with the dosing instructions. Further, it would not appear that the instant invention would cause a patient not to take bisphosphonates with food or a beverage other than water because that is up to the patient and would not be based on the arrangement of the medication. Therefore the instant invention would not affect a patient's compliance in this regard.

The Declarant, Stefan Van Der Geest, explains the details of a study he conducted to determine the advantages of the present invention. Four blister packs were given to the patients, each comprising one risendronate and six calcium tablets. One tablet, starting with the risendronate, was taken each day for four weeks. The study demonstrated that the instructions for administering the kit of the present invention are more easily understood than separate packs of bisphosphonate and calcium-containing supplement, and, therefore, the doses are properly administered and the benefits of treatment greatly increased.

The Examiner submits that this would not appear surprising because the blister pack includes the days for each dosage. Once a dosage is removed from the blister pack, a patient would know that the dosage was taken for the day and would not likely take another dose. Further Daifotis suggests using blister packs and discloses arranging the dosages in such a way that the bisphosphonate is taken on one day and a nutrient is taken the other days until another bisphosphonate is needed to be taken. Therefore the patient is more likely to follow the proper dosing procedure. It is further noted that the instructions disclosed on page 6 of the declaration are unclear, particularly step 5 which reads “Intake of calcium separate from the risendronate”. This instruction is unclear because it does not specifically indicate that calcium should not be taken on the same day as the risendronate. It would appear when a doctor is administering this combination to a patient that this would be clear. Further in regard to the blister pack, one of ordinary skill in the art would assume step 5 would be clear when given in conjunction with the blister pack to a patient because one tablet is to be taken a day and therefore the instruction would be clear and a patient would understand the instruction better. Therefore it is not unexpected that patient compliance in this regard is better.

The Declarant discloses that the kit of the present invention was preferred by the participants of the study, over the same medication from separate packs. Participants better understood the dosing instructions and patients are, therefore, more likely to comply with the instructions and benefit from treatment.

The Examiner submits that this finding is not unexpected. As noted above Daifotis in view of Kelly or Allendorf suggests placing the bisphosphonate and the nutrient in one blister pack so that a dosage is taken every day. These suggestions provide a convenient and effective way to carry out the methods of the disclosed invention (col. 13, lines 48-67). Providing each dosage in one blister pack, wherein it is instructed that only one pill a day is taken, would be expected to be preferred because the patient would less likely take the bisphosphonate on the same day as the calcium and there is only one package to keep up with for the week as oppose to two (when the bisphosphonate and the calcium are in separate packages). Further this method would lessen confusion and the instructions such as stated in 4 and 5 on page 6 of the declaration, which state “Intake of risedronate without other medications at the same time” and “Intake of calcium separate from the risendronate”, would appear more clear.

Declarant asserts that the significant benefits of the claimed invention are, at least: 1) a treatment regimen that includes calcium-containing supplementation with prescription medicine, which increases the probability that patients will receive both calcium (with or without vitamin D) and risedronate; and 2) improved patient understanding of dosing regimen to avoid incorrect intake, thereby leading to optimal absorption of risedronate and calcium (with or without vitamin D). Accordingly, the kit of the present invention meets a need in the market and leads to significantly superior results in the treatment of osteoporosis in patients taking bisphosphonates.

The Examiner submits that the blister packs suggested by Daifotis and disclosed by Kelly or Allendorf would address the problems disclosed by Declarant. Further, Daifotis recognizes these challenges and therefore suggests using blister packs, memory aids and placebos in order to help patients take the bisphosphonates correctly. The secondary references of Kelly and Allendorf disclose a blister pack that focuses on patient compliance for dosing and discloses using placebos in the same blister pack in order to make sure patients take the prescribed medication on the proper schedule. Therefore one of ordinary skill in the art would be aware of such uses of blister packs and it would have been obvious to use these types of blister packs disclosed by the secondary references to administer the bisphosphonate and nutrients of Daifotis to insure patients take the medication correctly. Accordingly based on the disclosure of Daifotis, Kelly, Allendorf and Palo Alto Medical Foundation, the invention of the instant claims is obvious and the findings of the Declaration do not appear to be unexpected.

Claims 1, 2, 4, 11, 14, 25 and 26 are rejected.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LEZAH ROBERTS whose telephone number is (571)272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lezah W Roberts/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612